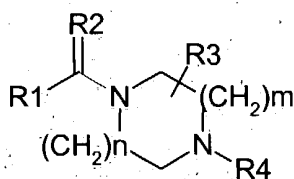


Claims

1. A novel aryl- or heteroaryl-substituted piperazinyldicarbonyl compound as in the general formula (1),

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1

- 10 where the substituents have the following meaning:

R1: fluoren-9-one, isoxazole, cinnoline, isothiazole, isoquinoline, 9H-fluorene, 9H-xanthene and 1H-pyrazole,

where the bonding can take place via any desired and possible ring member of the

- 15 heteroaryl or aryl radical and the aromatics and heteroaromatics can be mono- or polysubstituted or unsubstituted,

R2: O, S;

- 20 **R3:** represents one or up to 16 substituents selected from the group: H, unsubstituted or substituted alkyl, halogen, COOH, CONH₂,

where the substituents can be arranged vicinally or geminally on the heterocycle;

R4: unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl,

- 25 unsubstituted or substituted alkylaryl, unsubstituted or substituted alkylhetaryl;

m, n: 0-3.

2. An aryl- or heteroarylcarbonylpiperazine compound of the general formula (1) as claimed in claim 1, in which

"halogen" comprises the halogen atoms fluorine, chlorine, bromine and iodine,

5

"metal" comprises metal ions such as sodium, potassium, lithium, magnesium, calcium, zinc and manganese ions,

10 "alkyl" comprises acyclic saturated or unsaturated hydrocarbon radicals, having 1 to 20 C atoms, which can be branched or straight-chain and unsubstituted or mono- or polysubstituted, alkenyls having at least one C-C double bond and alkynyls at least one C-C triple bond,

15 "cycloalkyl" comprises cyclic hydrocarbons having 3-12 carbon atoms, which can be saturated or unsaturated, unsubstituted or substituted, whose binding to the compounds of the general formula (1) can take place via any desired and possible ring member of the cycloalkyl radical and the cycloalkyl radical can also be part of a bi- or polycyclic system,

20 "heterocyclyl" stands for a 3-, 4-, 5-, 6-, 7- or 8-membered cyclic organic radical, which is unsubstituted or mono- or polysubstituted, saturated or unsaturated, but not aromatic, which contains at least 1, optionally 2, 3, 4 or 5 heteroatoms, preferably nitrogen, oxygen and sulfur, where the heteroatoms are identical or different and whose bonding to the compounds of the general formula (1) can take place via any desired and possible ring member of the heterocyclyl radical, where the heterocycle can also be part of a bi- or
25 polycyclic system,

"aryl" denotes aromatic hydrocarbons, which are unsubstituted or mono- or polysubstituted, inter alia phenyls, naphthyls and anthracenyls, whose radicals can also be fused to further saturated, (partially) unsaturated or aromatic ring systems and whose bonding to the
30 compounds of the general formula (1) can take place via any desired and possible ring member of the aryl radical,

"heteroaryl" stands for a 5-, 6- or 7-membered cyclic aromatic radical, which is unsubstituted or mono- or polysubstituted, identically or differently, which contains at least 1, optionally also 2, 3, 4 or 5 heteroatoms, preferably nitrogen, oxygen and sulfur, where the heteroatoms are identical or different and whose bonding to the compounds of the general formula (1) can take place via any desired and possible ring member of the heteroaryl radical, where the heterocycle can also be part of a bi- or polycyclic system,

"alkylcycloalkyl", "alkylheterocyclyl", "alkylaryl" or "alkylheteroaryl" have the meanings defined for alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl and the cycloalkyl, heterocyclyl, aryl or heteroaryl radical is bonded to the compounds of the general formula (1) via a C1-8 – alkyl group.

"substituted" in connection with "alkyl", "alkenyl" and "alkynyl" can denote the substitution of a hydrogen radical by F, Cl, Br, I, CN, NH₂, NH-alkyl, NH-cycloalkyl, NH-aryl, NH-heteroaryl, NH-alkylaryl, NH-alkylheteroaryl, NH-heterocyclyl, NH-alkyl-OH, N(alkyl)₂, N(alkylaryl)₂, N(alkylheteroaryl)₂, N(heterocyclyl)₂, N(alkyl-OH)₂, NO, NO₂, SH, S-alkyl, S-cycloalkyl, S-aryl, S-heteroaryl, S-alkylaryl, S-alkylheteroaryl, S-heterocyclyl, S-alkyl-OH, S-alkyl-SH, S-alkyl, S-S-cycloalkyl, S-S-aryl, S-S-heteroaryl, S-S-alkylaryl, S-S-alkylheteroaryl, S-S-heterocyclyl, SS-alkyl-OH, S-S-alkyl-SH, S-S-alkyl-C(O)-NH-heterocyclyl, OH, O-alkyl, O-cycloalkyl, O-alkylcycloalkyl, O-aryl, O-heteroaryl, O-alkylaryl, O-alkylheteroaryl, O-heterocyclyl, O-alkylheterocyclyl, O-alkyl-OH, O-alkyl-O-alkyl, O-SO₂-N(alkyl)₂, O-SO₂-OH, O-SO₂-O-alkyl, O-SO₂-O-cycloalkyl, O-SO₂-O-heterocycloalkyl, O-SO₂-O-alkylcycloalkyl, O-SO₂-O-alkylheterocycloalkyl, O-SO₂-O-aryl, O-SO₂-O-heteroaryl, O-SO₂-O-alkylaryl, O-SO₂-O-alkylheteroaryl, O-SO₂-alkyl, O-SO₂-cycloalkyl, O-SO₂-heterocycloalkyl, O-SO₂-alkylcycloalkyl, O-SO₂-alkylheterocycloalkyl, O-SO₂-aryl, O-SO₂-heteroaryl, O-SO₂-alkylaryl, O-SO₂-alkylheteroaryl, O-C(O)-alkyl, O-C(O)-cycloalkyl, O-C(O)-heterocycloalkyl, O-C(O)-alkylcycloalkyl, O-C(O)-alkylheterocycloalkyl, O-C(O)-aryl, O-C(O)-heteroaryl, O-C(O)-alkylaryl, O-C(O)-alkylheteroaryl, O-C(O)-O-alkyl, O-C(O)-O-cycloalkyl, O-C(O)-O-heterocycloalkyl, O-C(O)-O-alkylcycloalkyl, O-C(O)-O-alkylheterocycloalkyl, O-C(O)-O-aryl, O-C(O)-O-heteroaryl, O-C(O)-O-alkylaryl, O-C(O)-O-alkylheteroaryl, O-C(O)-NH-alkyl, O-C(O)-NH-cycloalkyl, O-C(O)-NH-heterocycloalkyl, O-C(O)-NH-alkylcycloalkyl, O-C(O)-NH-alkylheterocycloalkyl, O-C(O)-NH-aryl, O-C(O)-NH-heteroaryl, O-C(O)-NH-alkylaryl, O-C(O)-NH-alkylheteroaryl, O-C(O)-N(alkyl)₂, O-C(O)-N(cycloalkyl)₂, O-C(O)-N(heterocycloalkyl)₂,

O-C(O)N(alkylcycloalkyl)₂, O-C(O)N(alkylheterocycloalkyl)₂, O-C(O)N(aryl)₂, O-C(O)N(heteroaryl)₂, O-C(O)N(alkylaryl)₂, O-C(O)N(alkylheteroaryl)₂, O-P(O)(OH)₂, O-P(O)(O-metal)₂, O-P(O)(O-alkyl)₂, O-P(O)(O-cycloalkyl)₂, O-P(O)(O-aryl)₂, O-P(O)(O-heteroaryl)₂, O-P(O)(O-alkylaryl)₂, O-P(O)(O-alkylheteroaryl)₂, O-P(O)(N-alkyl)₂(N-alkyl)₂, O-P(O)(N-cycloalkyl)₂(N-cycloalkyl)₂, O-P(O)(N-heterocycloalkyl)₂(N-heterocycloalkyl)₂, O-P(O)(N-aryl)₂(N-aryl)₂, O-P(O)(N-heteroaryl)₂(N-heteroaryl)₂, O-P(O)(N-alkylaryl)₂(N-alkylaryl)₂, O-P(O)(N-alkylheteroaryl)₂(N-alkylheteroaryl)₂, CHO, C(O)-alkyl, C(S)-alkyl, C(O)-aryl, C(S)-aryl, C(O)-alkylaryl, C(S)-alkylaryl, C(O)-heterocyclyl, C(O)-heteroaryl, C(O)-alkylheteroaryl, C(S)-heterocyclyl, CO₂H, CO₂-alkyl, CO₂-cyclyl, CO₂-heterocyclyl, CO₂-aryl, CO₂-heteroaryl, CO₂-alkylaryl, C(O)-NH₂, C(O)NH-alkyl, C(O)NH-aryl, C(O)NH-heterocyclyl, C(O)NH-alkylheterocyclyl, C(O)N(alkyl)₂, C(O)N(alkylaryl)₂, C(O)N(alkylheteroaryl)₂, C(O)N(heterocyclyl)₂, SO-alkyl, SO₂-alkyl, SO₂-aryl, SO₂-alkylaryl, SO₂-heteroaryl, SO₂-alkylheteroaryl, SO₂NH₂, SO₃H, CF₃, CHO, CHS, alkyl, cycloalkyl, aryl, alkylaryl, heteroaryl, alkylheterocyclyl and/or heterocyclyl, where in the case of polysubstituted radicals these can be polysubstituted either on different or on identical atoms and the polysubstitution can take place with the same or different substituents,

"substituted" in connection with aryl, heterocyclyl, heteroaryl, alkylaryl and cycloalkyl can mean the substitution of one or more hydrogen atoms of the ring system by F, Cl, Br, I, CN, NH₂, NH-alkyl, NH-aryl, NH-heteroaryl, NH-alkylaryl, NH-alkylheteroaryl, NH-heterocyclyl, NH-alkyl-OH, N(alkyl)₂, NC(O)alkyl, N(alkylaryl)₂, N(alkylheteroaryl)₂, N(heterocyclyl)₂, N(alkyl-OH)₂, NO, NO₂, SH, S-alkyl, S-aryl, S-heteroaryl, S-alkylaryl, S-alkylheteroaryl, S-heterocyclyl, S-alkyl-OH, S-alkyl-SH, OH, O-alkyl, O-cycloalkyl, O-alkylcycloalkyl, O-aryl, O-heteroaryl, O-alkylaryl, O-alkylheteroaryl, O-heterocyclyl, O-alkylheterocyclyl, O-alkyl-OH, O-alkyl-O-alkyl, O-SO₂-N(alkyl)₂, O-SO₂-OH, O-SO₂-O-alkyl, O-SO₂-O-cycloalkyl, O-SO₂-O-heterocycloalkyl, O-SO₂-O-alkylcycloalkyl, O-SO₂-O-alkylheterocycloalkyl, O-SO₂-O-aryl, O-SO₂-O-heteroaryl, O-SO₂-O-alkylaryl, O-SO₂-O-alkylheteroaryl, O-SO₂-alkyl, O-SO₂-cycloalkyl, O-SO₂-heterocycloalkyl, O-SO₂-alkylcycloalkyl, O-SO₂-alkylheterocycloalkyl, O-SO₂-aryl, O-SO₂-heteroaryl, O-SO₂-alkylaryl, O-SO₂-alkylheteroaryl, O-C(O)-alkyl, O-C(O)-cycloalkyl, O-C(O)-heterocycloalkyl, O-C(O)-alkylcycloalkyl, O-C(O)-alkylheterocycloalkyl, O-C(O)-aryl, O-C(O)-heteroaryl, O-C(O)-alkylaryl, O-C(O)-alkylheteroaryl, O-C(O)-O-alkyl, O-C(O)-O-cycloalkyl, O-C(O)-O-heterocycloalkyl, O-C(O)-O-alkylcycloalkyl, O-C(O)-O-alkylheterocycloalkyl, O-C(O)-O-aryl, O-C(O)-O-heteroaryl, O-C(O)-O-alkylaryl, O-C(O)-O-

alkylheteroaryl, O-C(O)NH-alkyl, O-C(O)NH-cycloalkyl, O-C(O)NH-heterocycloalkyl, O-C(O)NH-alkylcycloalkyl, O-C(O)NH-alkylheterocycloalkyl, O-C(O)NH-aryl, O-C(O)NH-heteroaryl, O-C(O)NH-alkylaryl, O-C(O)NH-alkylheteroaryl, O-C(O)N(alkyl)₂, O-C(O)N(cycloalkyl)₂, O-C(O)N(heterocycloalkyl)₂, O-C(O)N(alkylcycloalkyl)₂, O-C(O)N(alkylheterocycloalkyl)₂, O-C(O)N(aryl)₂, O-C(O)N(heteroaryl)₂, O-C(O)N(alkylaryl)₂, O-C(O)N(alkylheteroaryl)₂, O-P(O)(OH)₂, O-P(O)(O-metal)₂, O-P(O)(O-alkyl)₂, O-P(O)(O-cycloalkyl)₂, O-P(O)(O-aryl)₂, O-P(O)(O-heteroaryl)₂, O-P(O)(O-alkylaryl)₂, O-P(O)(O-alkylheteroaryl)₂, O-P(O)(N-alkyl)₂(N-alkyl)₂, O-P(O)(N-cycloalkyl)₂(N-cycloalkyl)₂, O-P(O)(N-heterocycloalkyl)₂(N-heterocycloalkyl)₂, O-P(O)(N-aryl)₂(N-aryl)₂, O-P(O)(N-heteroaryl)₂(N-heteroaryl)₂, O-P(O)(N-alkylaryl)₂(N-alkylaryl)₂, O-P(O)(N-alkylheteroaryl)₂(N-alkylheteroaryl)₂, CHO, C(O)-alkyl, C(S)-alkyl, C(O)-aryl, C(S)-aryl, C(O)-alkylaryl, C(S)-alkylaryl, C(O)-heterocyclyl, C(S)-heterocyclyl, CO₂H, CO₂-alkyl, CO₂-alkylaryl, C(O)-NH₂, C(O)NH-alkyl, C(O)NH-aryl, C(O)NH-heterocyclyl, C(O)N(alkyl)₂, C(O)N(alkylaryl)₂, C(O)N(alkylheteroaryl)₂, C(O)N(heterocyclyl)₂, SO-alkyl, SO₂-alkyl, SO₂-aryl, SO₂-alkylaryl, SO₂-heteroaryl, SO₂-alkylheteroaryl, SO₂NH₂, SO₃H, CF₃, CHO, CHS, alkyl, cycloalkyl, aryl, alkylaryl, heteroaryl, alkylheterocyclyl and/or heterocyclyl, where the substituents are identical or different and can occur in any desired and possible position of the aryl, heterocyclyl, heteroaryl, alkylaryl and cycloalkyl radical and where polysubstituted radicals can be polysubstituted with the same or with different substituents, either on different or on identical atoms.

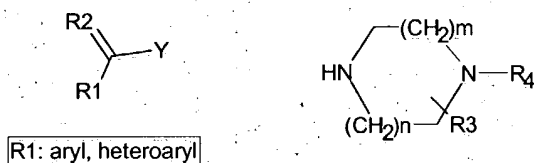
3. An aryl- or heteroarylcarbonylpiperazine compound of the general formula (1) as claimed in claims 1 and 2, wherein the alkyl radical can be methyl, ethyl, n-propyl, 2-propyl, n-butyl, sec.-butyl, tert.-butyl, n-pentyl, iso-pentyl, neo-pentyl, n-hexyl, 2-hexyl, n-octyl, ethylenyl (vinyl), ethynyl, propenyl (-CH₂CH=CH₂; -CH=CH-CH₃, -C(=CH₂)-CH₃), propynyl (-CH₂-C≡CH, -C≡C-CH₃), butenyl, butynyl, pentenyl, pentynyl, hexenyl, hexynyl, octenyl and octynyl.

4. An aryl- or heteroarylcarbonylpiperazine compound of the general formula (1) as claimed in claims 1 and 2, wherein the heterocyclyl radical can be tetrahydrofuryl, tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl.

5. An aryl- or heteroarylcarbonylpiperazine compound of the general formula (1) as claimed in claims 1 and 2, wherein the heteroaryl radical can be pyrrolyl, furyl, thienyl, thiazolyl, triazolyl, tetrazolyl, oxazolyl, isothiazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, triazinyl, benzothiazolyl, indolyl, indolizinyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, quinoxaliny, phthalazinyl, carbazolyl, phenazinyl, phenothiazinyl, purinyl, acridinyl, phenanthrinyl.
6. A compound of the general formula (1) as claimed in claims 1-5, wherein R₁, R₂, R₃, n and m have the abovementioned meanings and R₄ stands for phenyl, which is unsubstituted or substituted by one to five identical or different (C₁-C₆)-alkoxy groups, where adjacent oxygen atoms can also be linked by (C₁-C₂)-alkylene groups.
7. A compound of the general formula (1) as claimed in claims 1-5, wherein R, R₁, R₂, R₃, n and m have the abovementioned meanings and R₄ stands for 3,5-dimethoxyphenyl.
8. A compound of the general formula (1) as claimed in claims 1-5, wherein R, R₁, R₂, R₃, n and m have the abovementioned meanings and R₄ stands for 3-methoxyphenyl.
9. A physiologically tolerable salt of the compounds as in formula (1) as claimed in claims 1-8, comprised by neutralization of the basic compounds with inorganic and organic acids or neutralization of the acidic compounds with inorganic and organic bases, or its solvates and hydrates.
10. An aryl- or heteroarylcarbonylpiperazine compound of the general formula (1) as claimed in claims 1-9, having at least one asymmetric carbon atom, in the form of its racemates, in the form of the pure enantiomers and/or diastereomers or in the form of mixtures of these enantiomers and/or diastereomers or in the form of the tautomers.
11. A compound of the general formula (1), in particular one of the following compounds:
- 4-[4-(3,5-Dimethoxyphenyl)piperazine-1-carbonyl]fluoren-9-one (1)
- 4-[4-(6-methylpyridin-2-yl)piperazine-1-carbonyl]fluoren-9-one (2)
- 4-[4-(3-Hydroxyphenyl)piperazine-1-carbonyl]fluoren-9-one (3)

[4-(3,5-Dimethoxyphenyl)piperazin-1-yl]-(5-methyl-3-phenylisoxazol-4-yl)methanone (4)
 cinnolin-4-yl-[4-(3,5-dimethylphenyl)piperazin-1-yl]methanone (5)
 cinnolin-4-yl-[4-(6-methylpyridin-2-yl)piperazin-1-yl]methanone (6)
 (3,5-Bis-methylsulfanylisothiazol-4-yl)-[4-(6-methylpyridin-2-yl)piperazin-1-yl]methanone
 (7)
 [4-(3,5-Dimethoxyphenyl)piperazin-1-yl]-isoquinolin-1-ylmethanone (8)
 [4-(3,5-Dimethoxyphenyl)piperazin-1-yl]-(9H-fluoren-1-yl)methanone (9)
 (9H-Fluoren-9-yl)-[4-(3-methoxyphenyl)piperazin-1-yl]methanone (10)
 (9H-Fluoren-1-yl)-[4-(3-methoxyphenyl)piperazin-1-yl]methanone (11)
 [4-(3,5-Dimethoxyphenyl)piperazin-1-yl]-(9H-xanthen-9-yl)methanone (12)
 [4-(3-methoxyphenyl)piperazin-1-yl]-(9H-xanthen-9-yl)methanone (13)
 [4-(3-methoxyphenyl)piperazin-1-yl]-(2-phenyl-2H-pyrazol-3-yl)methanone (14)
 [4-(6-methylpyridin-2-yl)piperazin-1-yl]-(2-phenyl-2H-pyrazol-3-yl)methanone (15)
 [4-(3-Hydroxyphenyl)piperazin-1-yl]-(2-phenyl-2H-pyrazol-3-yl)methanone (16)
 [4-(3,5-Dimethoxyphenyl)piperazin-1-yl]-[1-(4-nitrophenyl)-5-trifluoromethyl-1H-pyrazol-4-yl]methanone (17)

12. A process for the preparation of aryl- and heteroarylcarbonylpiperazine compounds as claimed in one of claims 1 to 11, which comprises reacting a carboxylic acid of the general formula 2, in which R1 and R2 have the abovementioned meanings and Y stands for a leaving group such as halogen, hydroxyl, (C1-C6)-alkoxy, preferably methoxy and ethoxy, -O-tosyl, -O-mesyl, tetrazolyl or imidazolyl,



Formula 3.

with an amine of the general formula 3, in which R₄, m and n have the abovementioned meanings, optionally using a condensing agent and/or catalyst and diluents and auxiliaries with formation of the desired products.

13. The use of the aryl- and heteroarylcarbonylpiperazine compounds of the general formula (1) as claimed in one of claims 1 to 11 as therapeutic active compounds for the production of a medicament for the treatment of tumors in humans and in mammals.

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14. A medicament for use in the treatment of tumors in humans and in mammals, comprising at least one compound of the general formula (1) as claimed in one of claims 1 to 11, preferably together with customary pharmaceutically tolerable excipients, additives and vehicles.

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15. A medicament, comprising one or more compounds of the general formula (1) as claimed in one of claims 1-11 in addition to customary physiologically tolerable excipients, additives and vehicles.

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16. A process for the production of a medicament as claimed in claim 15, which comprises processing one or more aryl- and heteroarylcarbonylpiperazine compounds of the general formula (1) as claimed in one of claims 1-11 with customary pharmaceutical vehicles and/or diluents or other excipients to give pharmaceutical preparations, or bringing them into a therapeutically administrable form.

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17. A process for the treatment of benign and malignant tumors in humans and mammals, which comprises administering at least one compound of the general formula (1) as claimed in one of claims 1 to 11 to the human or mammal into a dose effective for tumor treatment.

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